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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/737,335	06/13/01	GHONE	P/717-189

022352
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HM22/1106

EXAMINER	
HAMUD,F	
ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 11/06/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

File copy

Office Action Summary

Application No.	Applicant(s)
09/787,335	Grone et al.
Examiner	**Art Unit**
Fozia Hamud	1647

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) [X] Responsive to communication(s) filed on *Aug 27, 2001*.

2a) [ ] This action is **FINAL.** 2b) [X] This action is non-final.

3) [ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) [X] Claim(s) *1-16* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) [ ] Claim(s) _____ is/are allowed.

6) [X] Claim(s) *1-16* is/are rejected.

7) [ ] Claim(s) _____ is/are objected to.

8) [ ] Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) [ ] The specification is objected to by the Examiner.

10) [ ] The drawing(s) filed on _____ is/are objected to by the Examiner.

11) [ ] The proposed drawing correction filed on _____ is: a) [ ] approved b) [ ] disapproved.

12) [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) [X] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) [X] All b) [ ] Some* c) [ ] None of:

1. [ ] Certified copies of the priority documents have been received.
2. [ ] Certified copies of the priority documents have been received in Application No. _____.
3. [X] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) [ ] Notice of References Cited (PTO-892)
16) [X] Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) [X] Information Disclosure Statement(s) (PTO-1449) Paper No(s). 6
18) [ ] Interview Summary (PTO-413) Paper No(s). _____
19) [ ] Notice of Informal Patent Application (PTO-152)
20) [ ] Other: _____

DETAILED ACTION

1. Claims 1-16 are pending and under consideration by the Examiner.

Specification

2a. It is noted that this application appears to claim subject matter disclosed in prior PCT Application No. PCT/EP99/06844 filed on 16 September 1999, now WO 00/16796 issued on 30 March 2000. A reference to the prior application must be inserted as the first sentence of the specification of this application if Applicant intends to rely on the filing date of the prior application under 35 U.S.C. 120. See 37 CFR 1.78(a).

It is suggested that below the title of the invention be inserted:

Cross Reference to Related Applications

"This Application is a 371 of WO 00/16796".

Appropriate correction is required.

2b. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b).

An abstract on a separate sheet is required.

2c. The following guidelines illustrate the preferred layout and content for patent applications. These guidelines are suggested for the applicant's use.

Claim Rejections - 35 U.S.C. § 101

3. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3a. Claims 1-8 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 1-8 recite "Use of a chemokine receptor antagonist in.....", however there are no provisions for "use" language in the statute. Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4a. Claims 1-16, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating or preventing the rejection of renal allograft transplantation by administering a pharmaceutical composition comprising the chemokine receptor antagonist Met-RANTES and cyclosporin and a pharmaceutical composition comprising Met-RANTES and cyclosporin, does not reasonably provide enablement for a method of treating or preventing the rejection of transplanted organs, tissues or cells by administering a pharmaceutical composition comprising "all possible" chemokine receptor antagonist and cyclosporin or a pharmaceutical composition comprising "all possible" chemokine receptor antagonists and cyclosporin, or wherein said chemokine receptor antagonist is amino-terminally truncated. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1 and 9 recite " use of a chemokine receptor antagonist in combination with a cyclosporin ...for treating or preventing the rejection of transplanted organs, tissues or cells ..." and "a pharmaceutical composition containing a chemokine receptor antagonist in combination with a

cyclosporin ...for treating or preventing the rejection of transplanted organs, tissues or cells .", respectively, what is claimed in the instant invention broadly encompass pharmaceutical compositions comprising "all" chemokine receptor antagonists in combination with a cyclosporin and a method of using said pharmaceutical composition for treating or preventing the rejection of transplanted organs, tissues or cells. While the specification discloses that Met-RANTES in combination with low dose of cyclosporin caused significant reduction of interstitial rejection of renal allograft transplantation, significant reduction in the vascular and tubular damage and significant reduction in mononuclear cell infiltration, (see page 4, lines 16-27, page 16, lines 11-27 and table 2 and 3). Thus the only chemokine receptor antagonist used in combination with cyclosporin for the treatment and prevention of the rejection of transplanted kidney, is Met-RANTES. The physiological effects of chemokines receptors are diverse, and one of ordinary skill in the art would not expect antagonism of any chemokine receptor to result in the reduction of graft rejection. Therefore, the specification is non-enabling for the unlimited number chemokine receptor antagonists (amino-terminally truncated, extended or full length) encompassed by the scope of the claims to be used in combination with cyclosporin, because not all chemokine receptors are involved in the rejection of transplants. The claimed invention encompasses chemokine receptor antagonists not envisioned or described in the specification, and neither does the specification disclose whether these claimed chemokine receptor antagonists in combination with cyclosporin would have beneficial or detrimental effects on organ transplant patients. The specification discloses that adding a single methionine at the N-terminus of RANTES changes the agonist protein into a RANTES receptor antagonist with nonmolar potency, and that treatment of rat renal transplant model with Met-RANTES in combination with low dose cyclosporin

caused a significant reduction of interstitial rejection in renal allograft transplantation, (page 16). Thus the only amino-terminally extended chemokine receptor antagonist to be used in combination with cyclosporin, disclosed by Applicants is Met-RANTES. The specification describes the specific chemokine receptor antagonist Met-RANTES which has specific characteristics and properties. These properties differ structurally, chemically and physically from other known chemokine receptor antagonists. The criteria set forth in Ex parte Forman (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in In re Wands (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims, is the basis for determining undue extermination. In the instant application, the only chemokine receptor antagonist disclosed and used in combination with cyclosporin for the treatment and prevention of renal transplant rejection is Met-RANTES, and the skilled artisan would not be able to predict if other chemokine receptor antagonists in combination with cyclosporin would have any significant effect on organ transplant rejection, whether they would have beneficial or detrimental effects on patients. There is no guidance that "all" chemokine receptor antagonists would function the way Met-RANTES did, neither does the specification provide any guidance of how many amino acids to delete from the N-terminus, how many amino acids to add to the N-terminus of said chemokine receptor antagonists. Furthermore, instant specification only demonstrates that Met-RANTES in combination with low dose of cyclosporin caused significant

reduction of interstitial rejection of renal allograft transplantation, and does not show that said pharmaceutical composition would be effective against rejection of other transplanted organs.

Thus, Applicants are only enabled for a method of treating or preventing the rejection of renal allograft transplantation by administering a pharmaceutical composition comprising the chemokine receptor antagonist Met-RANTES in combination with cyclosporin and a pharmaceutical composition comprising Met-RANTES and cyclosporin.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-8, 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5a. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: there is no recitation in the claim of what are the steps to be followed to produce the claimed pharmaceutical composition, how much of the chemokine receptor antagonist and how of much of the cyclosporin should be used? Should the produced pharmaceutical composition be in a liquid form, in a solid form or in a powder form? Should the active ingredients of said pharmaceutical composition be put together in a certain order? Appropriate c correction is required.

5b. Claim 2 which recites "...wherein the chemokine receptor antagonist and the cyclosporin are used simultaneously, separately or sequentially", is vague and indefinite because, it is unclear how the

pharmaceutical composition produced in claim 1, can be used simultaneously, separately or sequentially? The pharmaceutical composition recited in claim 1 is produced from a combination of chemokine receptor antagonist and a cyclosporin, it appears that once the chemokine receptor antagonist and the cyclosporin are combined, they become one composition, therefore, it is unclear how could the ingredients of said pharmaceutical composition be used simultaneously, separately or sequentially?

5c. Claims 8 and 16 recite "...for treating or preventing renal allograft transplantation.", however, the claims were probably meant to recite ".....for treating or preventing renal allograft transplant rejection". Appropriate correction is required. Appropriate correction is required.

Claims 3-7 are rejected as being vague and indefinite for so long as they depend to claim 1 for the limitation set forth directly above.

Conclusion

No claim is allowed.

A pharmaceutical composition comprising Met-RANTES and cyclosporin and a method of using said pharmaceutical composition for treating or preventing renal allograft transplant rejection are free of the prior art of record.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia Hamud whose telephone number is (703) 308-8891. The examiner can normally be reached on Monday, Wednesday-Thursday from 6:30AM to 4:00PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Art Unit: 1647

Official papers filed by fax should be directed to (703) 308-4227. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Fozia Hamud
Patent Examiner
Art Unit 1647
29 October 2001

CHRISTINE J. SAOUD
PRIMARY EXAMINER
Christine J. Saoud

Attachment for PTO-948 (Rev. 03/01, or earlier)
6/18/01

The below text replaces the pre-printed text under the heading, "Information on How to Effect Drawing Changes," on the back of the PTO-948 (Rev. 03/01, or earlier) form.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

1. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the Notice of Allowability. Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136(a) or (b) for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

2. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit the drawing corrections within the time period set in the attached Office communication. See 37 CFR 1.85(a).

Failure to take corrective action within the set period will result in **ABANDONMENT** of the application.